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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/600,070	06/20/2003	Katherine W. Osteryoung	MSU-08153	5938

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EXAMINER	
KUBELIK, ANNE R	
ART UNIT	**PAPER NUMBER**
1638	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/600,070	OSTERYOUNG ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 June 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 23-30 are pending.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

3. Claims 23-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Neither the instant specification nor the originally filed claims appear to provide support for vectors comprising any nucleic acids encoding proteins of amino acids 747-801, amino acids 679-799, amino acids 623-691, amino acids 316-381, amino acids 244-277, amino acids 186-221, and amino acids 95-121 of SEQ ID NO:2.

The specification on pg 92-93 (Table 3), pointed to for support on pg 4 of Applicant's response filed 16 August 2007, mentions protein fragments with BLAST similarity to amino acids 747-801, amino acids 244-277 or amino acids 95-121 of SEQ ID NO:2, but these do not provide support for any actual protein comprising those amino acids, much less one that function in division of a photosynthetic prokaryote or a plastid. The specification provides no support for any protein comprising amino acids 679-799, amino acids 623-691, amino acids 316-381, and amino acids 186-221 of SEQ ID NO:2.

Thus, such vectors constitute NEW MATTER. In response to this rejection, Applicant is required to point to support for vectors or to cancel the new matter.

4. Claims 23-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding SEQ ID NO:2, does not reasonably provide enablement for a vector comprising any nucleic acid that is at least 90% homologous to SEQ ID NO:1 or 3, wherein the nucleic acid encodes a product that functions in photosynthetic prokaryote or plastid division, and cells, plants and seeds transformed with it. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. Due to Applicant's amendment of the claims, the rejection is modified from the rejection set forth in the Office action mailed 14 May 2007. Applicant's arguments filed 16 August 2007 have been fully considered but they are not persuasive.

The claims are broadly drawn to a vector comprising any nucleic acids encoding proteins of amino acids 747-801, amino acids 679-799, amino acids 623-691, amino acids 316-381, amino acids 244-277, amino acids 186-221, or amino acids 95-121 of SEQ ID NO:2, wherein the nucleic acid encodes a product that functions in photosynthetic prokaryote or plastid division, and cells, plants and seeds transformed with it.

The instant specification, however, only provides guidance for isolation of Ftn2 from *Synechococcus* and identification of putative cyanobacterial homologs (examples 4 and 5), which has 17% identity to an unknown protein (SEQ ID NO:2, encoded by the genomic sequence SEQ ID NO:3 and cDNA SEQ ID NO:1) in *Arabidopsis*; mapping the *arc6* mutation in *Arabidopsis* to

show that it and the unknown protein map to chromosome 5 (example 2); rescuing the *arc6* mutation by SEQ ID NO:1 (example 2); analysis of the mutant to show that FtsZ rings and filaments are disrupted (example 2); identification of potential Ftn2 homologues from various database sequences (example 3); isolation of an Ftn2 gene from Synechococcus by transposon mutagenesis (examples 4-5); identification of arc5 (examples 6) and Fzo-like (example 7) genes from *Arabidopsis*. The specification teaches that SEQ ID NO:2 does not have a proper DnaJ domain or a complete myb domain, but appears to have a chloroplast targeting sequence and three putative transmembrane helices (pg 90-91).

The instant specification fails to teach how to make the full scope of nucleic acids encoding proteins of amino acids 747-801, amino acids 679-799, amino acids 623-691, amino acids 316-381, amino acids 244-277, amino acids 186-221, or amino acids 95-121 of SEQ ID NO:1, wherein the nucleic acid encodes a product that functions in photosynthetic prokaryote or plastid division.

The claimed nucleic acids encode proteins with only 27 to 122 amino acids of SEQ ID NO:2; the remainder of the protein, if there is any at all, can be of any sequence. Thus, the claims encompass nucleic acids encoding a 27 amino acid long fragment of SEQ ID NO:2 and nucleic acids encoding proteins with up to 774 amino acid substitutions relative to the 801 amino acid long SEQ ID NO:2. These latter proteins would have 3.4% identity to SEQ ID NO:2.

The instant specification fails to provide sufficient guidance for which 774 amino acids of SEQ ID NO:2 can be altered and to which other amino acids, and which amino acids must not be changed, to maintain photosynthetic prokaryote or plastid division activity of the encoded

protein. The specification also fails to provide adequate guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional enzyme.

The guidance in the specification with respect to making amino acid substitutions in SEQ ID NO:2 is as follows: Homologs have Dna-J-like domain missing the central HPD motif, a putative myb domain, a TPR repeat and a leucine zipper, although neither of the latter are in SEQ ID NO:2 (pg 59, line 23, to pg 62, line 2).

Variants include mutants, fragments, fusion proteins and functional equivalents, and changes that result in altered regulatory or enzymatic activity. Includes substitutions, deletions and additions. Conservative amino acid substitutions are suggested as not having a major effect on the biological activity of the protein, but nonconservative substitutions are contemplated, as are amino acid deletions and insertions. Methods of making include site-directed, random mutagenesis and gene shuffling (pg 55, line 22, to pg 59, line 20).

Lastly, Examples 3 and Fig 3 show putative homologs , which have 15-47% identity to SEQ ID NO:2 (Table 4). Most of the homologs are fragments encoded by ESTs (See Table 3).

Thus, from the guidance in the specification, it would appear that the vast majority of the amino acids in SEQ ID NO:2 could be substituted with any other amino acid.

Making amino acid substitutions in SEQ ID NO:2 is unpredictable.

Making "conservative" substitutions (*e.g.*, substituting one polar amino acid for another, or one acidic one for another) does not produce predictable results. Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252) showed that the "conservative" substitution of glutamic acid for aspartic acid

at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitutions with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach that when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see Table 1).

Guo et al (2004, Proc. Natl. Acad. Sci. USA 101: 9205-9210) teach that while proteins are fairly tolerant to mutations resulting in single amino acid changes, increasing the number of substitutions additively increases the probability that the protein will be inactivated (pg 9209, right column, paragraph 2). Thus, making and analyzing proteins with 366 amino acid substitutions that also have Ftn2 activity would require undue experimentation.

Further, the claimed fragments of SEQ ID NO:2, that is amino acids 747-801, amino acids 679-799, amino acids 623-691, amino acids 316-381, amino acids 244-277, amino acids 186-221, and amino acids 95-121, would not have the function of SEQ ID NO:2.

The Dna-J-like domain missing the central HPD motif spans amino acids 89-153 of SEQ ID NO:2 and the putative myb domain spans amino acids 677-690 of SEQ I NO:2 (specification, pg 59, line 23, to pg 62, line 2). None of the fragments encompass both of these. Further, it is unliklekt that a 27 to 121 amino acid fragment of a 801 amino acid long protein would have the same function as that protein.

The only assay for FTN2 function is complementation of the arc6 mutation with a nucleic

acid encoding SEQ ID NO:2 (example 2). It is not clear that other nucleic acids encoding proteins with 366 amino acid substitutions relative to SEQ ID NO:2 would be able to complement this mutant, given the importance of individual amino acids in portion-protein interactions.

Additionally, even 5 years after the filing of the instant application, the function of Ftn2 is not known (Maple et al, Annals Botany 99:565-579; pg 570, right column, paragraph 2). Also, Arc6 (the instant SEQ ID NO:2) appears to have a very different function in plants than Ftn2 does in prokaryotes (pg 570, right column, paragraph , to pg 571, right column, paragraph 2).

Thus, extensive teachings are required for making nucleic acids encoding Ftn2 proteins with 774 amino acid substitutions relative to SEQ ID NO:2 or that are as small as 27 amino acids of SEQ ID NO:1, as encompassed by the claimed nucleic acids. These teachings are not provided for by the specification. The specification also fails to overcome the unpredictability of making large numbers of amino acid substitutions in SEQ ID NO:2 as it provides no working examples of proteins with 744 amino acid substitutions relative to SEQ ID NO:2.

The specification also does not teach how to use plants in which Ftn2 is overexpressed. The phenotype of such plants is not taught; thus one of skill in the art would not know how to use them.

As the specification does not describe the transformation of any plant with nucleic acid encoding Ftn2 proteins with 774 amino acid substitutions relative to SEQ ID NO:2 or that are as small as 27 amino acids of SEQ ID NO:1, undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed by the claims and plants

transformed therewith, to identify those with an unspecified phenotype.

Given the claim breath, unpredictability in the art, undue experimentation, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

Applicant urges that the examiner has misinterpreted the claim scope because the triplet coding pattern was not taken into account (response pg 3).

This is not found persuasive because a nucleic acid with 240 substitutions can have them in 240 different codons, and each of these substitutions can change the amino acid encoded at that position. The instant claim encompass nucleic acids encoding proteins with 774 amino acid substitutions relative to SEQ ID NO:2. The specification does not teach how to make the claimed nucleic acids.

Applicant urges that the claim amendments better define the embodiment (response pg 4).

This is not found persuasive for the reasons detailed in the rejection above.

5. Claims 23-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Due to Applicant's amendment of the claims, the rejection is modified from the rejection set forth in the Office action mailed 14 May 2007, as applied to claims 23-30. Applicant's

arguments filed 16 August 2007 have been fully considered but they are not persuasive.

The essential feature of the claims is a nucleic acid that encodes protein of amino acids 747-801, amino acids 679-799, amino acids 623-691, amino acids 316-381, amino acids 244-277, amino acids 186-221, or amino acids 95-121 of SEQ ID NO:2, wherein the nucleic acid encodes a product that functions in photosynthetic prokaryote or plastid division. As the protein of SEQ ID NO:2 and its activity are novel, there is no well-developed field of prior art.

The specification describes FTN2 function as a protein that when its levels are decreased leads to incomplete or no division of a prokaryote or plastid, resulting in long filamentous cells in cyanobacteria and single or few very large chloroplasts in plants (pg 15, lines 1-10).

The specification describes Ftn2 proteins as having a DnaJ-like domain at its N-terminal half, but that this domain is missing the essential central HPD motif (pg 60, lines 7-10; pg 90, lines 12-17). Other motifs are described (pg 60, lines 11-20; pg 90, lines 17-27; Table 7), but such motifs are not present in every protein indicated to be an Ftn2 homolog.

There is no description of the structure required for the recited function, and no description of the necessary and sufficient structural elements of a protein with Ftn2 function.

The only species described in the specification are SEQ ID NOs:3 and 4, which encode SEQ ID NOs:2 and 5, respectively. The putative homologs described in the specification are partial sequences whose function has not been determined.

One of skill in the art would not recognize that Applicant was in possession of the necessary common attributes or features of the genus in view of the disclosed species. Since the disclosure fails to describe the common attributes that identify members of the genus, and

because the genus is highly variant, SEQ ID NOs:1, 3 and 4 are insufficient to describe the claimed genus.

Hence, Applicant has not, in fact, described a nucleic acid that encodes protein of amino acids 747-801, amino acids 679-799, amino acids 623-691, amino acids 316-381, amino acids 244-277, amino acids 186-221, or amino acids 95-121 of SEQ ID NO:2, wherein the nucleic acid encodes a product that functions in photosynthetic prokaryote or plastid division, within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and functional characteristics of the claimed compositions, it is not clear that Applicant was in possession of the claimed genus at the time this application was filed.

Applicant urges that they disagree for the reason above and that their claim amendments make the claims allowable (response pg 4).

This is not found persuasive for the reasons detailed above.

6. Claim 29 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. The rejection is modified from the rejection from the rejection set forth in the Office action mailed 14 May 2007. Applicant's arguments filed 16 August 2007 have been fully considered but they are not persuasive.

It is not clear in claim 29 if the plant seed comprises the heterologous gene. Not all seeds

of a transgenic plant will comprise the nucleic acid with which the plant has been transformed. .

Applicant urges that the amendment obviates the rejection (response pg 5).

This is not found persuasive for the reasons above.

Conclusion

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached at (571) 272-0975.

The central fax number for official correspondence is (571) 273-8300.

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Anne Kubelik, Ph.D.
October 12, 2007

/Anne Kubelik/
Primary Examiner